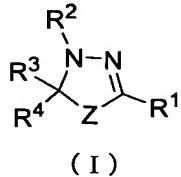


What is claimed is:

1. An antitumor agent comprising a thiadiazoline derivative represented by the general formula (I), or a pharmacologically acceptable salt thereof as an active ingredient:



<wherein Z represents a sulfur atom or -S(=O)-, R¹ represents substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted aryl, a substituted or unsubstituted aromatic heterocyclic group, or -C(=W)R⁵ {wherein W represents an oxygen atom or a sulfur atom, and R⁵ represents a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, -YR⁶ (wherein Y represents an oxygen atom or a sulfur atom, and R⁶ represents a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic group), or -NR⁷R⁸ [wherein R⁷ and R⁸ are the same or different, and represent a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, a substituted or unsubstituted heterocyclic group, -OR⁹ (wherein R⁹ has the same meaning as that of the aforementioned R⁶), or -NR¹⁰R¹¹ (wherein R¹⁰ and R¹¹ are the same or different, and represent a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic group, or R¹⁰ and R¹¹ are combined together with the adjacent nitrogen atom to form a substituted or unsubstituted heterocyclic group], or R⁷ and R⁸ are combined together with the adjacent nitrogen atom to form a substituted or unsubstituted heterocyclic group]},

R² represents a hydrogen atom, substituted or unsubstituted lower alkyl, or -C(=W¹)R¹² [wherein W¹ represents an oxygen atom or a sulfur atom, R¹² represents a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, a substituted or unsubstituted heterocyclic group, -Y¹R¹³ (wherein Y¹ represents an oxygen atom or a sulfur atom, and R¹³ represents substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic group), or -NR¹⁴R¹⁵ (wherein R¹⁴ and R¹⁵ are the same or different, and represent a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic group), or R¹⁴ and R¹⁵ are combined together with the adjacent nitrogen atom to form a substituted or unsubstituted heterocyclic group)],

R³ represents a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic group, and

R⁴ represents substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic group,

or R³ and R⁴ are combined together to represent

-(CR^{16A}R^{16B})_{m1}-Q-(CR^{16C}R^{16D})_{m2}- {wherein Q represents a single bond, substituted or unsubstituted phenylene, or cycloalkylene, m₁ and m₂ are the same or different, and each represents an integer of 0 to 4, with the proviso that m₁ and m₂ are not 0 at the same time},

R^{16A}, R^{16B}, R^{16C} and R^{16D} are the same or different, and represent a hydrogen atom, halogen, substituted or unsubstituted lower alkyl, -OR¹⁷ [wherein R¹⁷ represents a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic group],

or unsubstituted cycloalkyl, substituted or unsubstituted aryl, a substituted or unsubstituted heterocyclic group, -CONR¹⁸R¹⁹ (wherein R¹⁸ and R¹⁹ are the same or different, and represent a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic group, or R¹⁸ and R¹⁹ are combined together with the adjacent nitrogen atom to form a substituted or unsubstituted heterocyclic group),

-SO₂NR²⁰R²¹ (wherein R²⁰ and R²¹ have the same meanings as those of the aforementioned R¹⁸ and R¹⁹, respectively), or -COR²² (wherein R²² represents a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic group)], -NR²³R²⁴ [wherein R²³ and R²⁴ are the same or different, and represent a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, a substituted or unsubstituted heterocyclic group, -COR²⁵ (wherein R²⁵ represents a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, a substituted or unsubstituted heterocyclic group, substituted or unsubstituted lower alkoxy, substituted or unsubstituted aryloxy, amino, substituted or unsubstituted lower alkylamino, di-(substituted or unsubstituted lower alkyl)amino, or substituted or unsubstituted arylamino), or -SO₂R²⁶ (wherein R²⁶ represents substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic group), or R²³ and R²⁴ are combined together with the adjacent nitrogen atom to form a substituted or unsubstituted heterocyclic group], or -CO₂R²⁷ (wherein R²⁷ represents a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or a substituted or unsubstituted

heterocyclic group), or R^{16A} and R^{16B} , or R^{16C} and R^{16D} are combined together to represent an oxygen atom, and when m_1 or m_2 is an integer of 2 or more, any of R^{16A} , R^{16B} , R^{16C} and R^{16D} may be the same or different, and any two of R^{16A} , R^{16B} , R^{16C} and R^{16D} which are bound to the adjacent two carbon atoms may combine together to form a bond}>.

2. The antitumor agent according to claim 1, wherein R^1 is substituted or unsubstituted lower alkynyl, substituted or unsubstituted aryl, or a substituted or unsubstituted aromatic heterocyclic group.

3. The antitumor agent according to claim 1, wherein R^1 is substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, or $\cdot C(=W)R^5$ (wherein W and R^5 have the same meanings as those mentioned above).

4. The antitumor agent according to claim 1, wherein R^1 is substituted or unsubstituted aryl, or a substituted or unsubstituted aromatic heterocyclic group.

5. The antitumor agent according to claim 1, wherein R^1 is substituted or unsubstituted aryl.

6. The antitumor agent according to claim 1, wherein R^1 is substituted or unsubstituted lower alkynyl.

7. The antitumor agent according to claim 1, wherein R^1 is substituted or unsubstituted lower alkyl, or substituted or unsubstituted lower alkenyl.

8. The antitumor agent according to any one of claims 1 to 7, wherein R^2 is a hydrogen atom, substituted or unsubstituted lower alkyl, or $\cdot C(=W^1)R^{12}$ (wherein W^1 and R^{12} have the same meanings as those mentioned above, respectively).

9. The antitumor agent according to any one of claims 1 to 7, wherein R^2 is $\cdot C(=W^1)R^{12}$ (wherein W^1 and R^{12} have the same meanings as those mentioned above, respectively).

10. The antitumor agent according to claim 8 or 9, wherein R^{12} is substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, or substituted or unsubstituted cycloalkyl.

11. The antitumor agent according to claim 8 or 9, wherein R^{12} is substituted or unsubstituted lower alkyl.

12. The antitumor agent according to claim 8 or 9, wherein R^{12} is lower alkyl.

13. The antitumor agent according to any one of claims 8 to 12, wherein W^1 is an oxygen atom.

14. The antitumor agent according to any one of claims 1 to 13, wherein R³ is substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic group.

15. The antitumor agent according to any one of claims 1 to 13, wherein R³ is substituted or unsubstituted lower alkyl.

16. The antitumor agent according to any one of claims 1 to 13, wherein R³ is substituted lower alkyl.

17. The antitumor agent according to any one of claims 1 to 16, wherein R⁴ is substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic group.

18. The antitumor agent according to any one of claims 1 to 16, wherein R⁴ is substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic group.

19. The antitumor agent according to any one of claims 1 to 16, wherein R⁴ is substituted or unsubstituted phenyl, or substituted or unsubstituted thienyl.

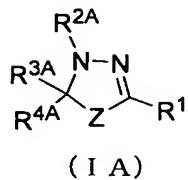
20. The antitumor agent according to any one of claims 1 to 13, wherein R³ and R⁴ are combined together to represent -(CR^{16A}R^{16B})_{m1}-Q-(CR^{16C}R^{16D})_{m2}- (wherein Q, R^{16A}, R^{16B}, R^{16C}, R^{16D}, m1 and m2 have the same meanings as those mentioned above, respectively).

21. The antitumor agent according to any one of claims 1 to 13, wherein R³ and R⁴ are combined together to represent -(CH₂)_{m1}-Q-(CH₂)_{m2}- (wherein Q, m1 and m2 have the same meanings as those mentioned above, respectively).

22. The antitumor agent according to claim 20 or 21, wherein Q is substituted or unsubstituted phenylene.

23. A mitotic kinesin Eg5 inhibitor comprising the thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 1 to 22 as an active ingredient.

24. A thiadiazoline derivative represented by the formula (IA) or a pharmacologically acceptable salt thereof:



{wherein Z has the same meaning as that mentioned above,

R¹ has the same meaning as that mentioned above,

(A) when R¹ is substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, or -C(=W)R⁵ (wherein W and R⁵ have the same meanings as those mentioned above, respectively), R^{2A}, R^{3A} and R^{4A} have the same meanings as those of the aforementioned R², R³ and R⁴ (with proviso that Z^A is a sulfur atom, R¹ is benzyl, R^{2A} is acetyl, one of R³ and R^{4A} is methyl, and the other of R³ and R^{4A} is not 2-oxopropyl), respectively

(B) when R¹ is substituted or unsubstituted lower alkynyl, or a substituted or unsubstituted aromatic heterocyclic group, R^{2A} and R^{3A} have the same meanings as those of the aforementioned R² and R³, respectively, and R^{4A} represents substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic group, and

(C) when R¹ is substituted or unsubstituted aryl, R^{2A} represents -C(=W)R¹² (wherein W and R¹² have the same meanings as those mentioned above, respectively), R^{3A} represents -(CH₂)_kNHSO₂R^{3B} [wherein k represents an integer of 1 to 6, and R^{3B} represents substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, or -NR^{7B}R^{8B} (wherein R^{7B} and R^{8B} have the same meanings as those of the aforementioned R⁷ and R⁸, respectively)], -(CH₂)_kNR^{7C}R^{8C} (wherein k has the same meaning as that mentioned above, and R^{7C} and R^{8C} have the same meanings as those of the aforementioned R⁷ and R⁸, respectively), or -(CH₂)_kNHC(=O)R^{7D} (wherein k has the same meaning as that mentioned above, and R^{7D} has the same meaning as that of the aforementioned R⁷), and R^{4A} has the same meaning as that of the aforementioned R⁴}.

25. The thiadiazoline derivative or a pharmacologically acceptable salt thereof according to claim 24, wherein Z is a sulfur atom.

26. The thiadiazoline derivative or a pharmacologically acceptable salt thereof according to claim 24 or 25, wherein R¹ is substituted or unsubstituted lower alkynyl, substituted or unsubstituted aryl, or a substituted or unsubstituted aromatic heterocyclic group.

27. The thiadiazoline derivative or a pharmacologically acceptable salt thereof according to claim 24 or 25, wherein R¹ is substituted or unsubstituted aryl.

28. The thiadiazoline derivative or a pharmacologically acceptable salt thereof according to claim 24 or 25, wherein R¹ is substituted or unsubstituted phenyl.

29. The thiadiazoline derivative or a pharmacologically acceptable salt thereof according to claim 24 or 25, wherein R¹ is substituted or unsubstituted lower alkynyl.

30. The thiadiazoline derivative or a pharmacologically acceptable salt thereof according to claim 24 or 25, wherein R¹ is substituted lower alkyl.

31. The thiadiazoline derivative or a pharmacologically acceptable salt thereof according to claim 24 or 25, wherein R¹ is -C(=W)R⁵ (wherein W and R⁵ have the same meanings as those mentioned above, respectively).

32. The thiadiazoline derivative or a pharmacologically acceptable salt thereof according to claim 31, wherein W is an oxygen atom.

33. The thiadiazoline derivative or a pharmacologically acceptable salt thereof according to claim 31 or 32, wherein R⁵ is -NR⁷R⁸ (wherein R⁷ and R⁸ have the same meanings as those mentioned above, respectively).

34. The thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 24 to 33, wherein R^{2A} is -C(=O)R¹² (wherein R¹² have the same meanings as those mentioned above).

35. The thiadiazoline derivative or a pharmacologically acceptable salt thereof according to claim 34, wherein R¹² is lower alkyl.

36. The thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 24 to 35, wherein R^{3A} is substituted or unsubstituted lower alkyl.

37. The thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 24 to 35, wherein R^{3A} is -(CH₂)_kNHSO₂R^{3B} (wherein k and R^{3B} have the same meanings as those mentioned above, respectively), -(CH₂)_kNR^{7C}R^{8C} (wherein k, R^{7C} and R^{8C} have the same meanings as those mentioned above, respectively), or -(CH₂)_kNHC(=O)R^{7D} (wherein k and R^{7D} have the same meanings as those mentioned above, respectively).

38. The thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 24 to 35, wherein R^{3A} is -(CH₂)_kNHSO₂R^{3B}

(wherein k and R^{3B} have the same meanings as those mentioned above, respectively).

39. The thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 24 to 38, wherein R^{4A} is substituted or unsubstituted aryl, or a substituted or unsubstituted aromatic heterocyclic group.

40. The thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 24 to 38, wherein R^{4A} is substituted or unsubstituted aryl.

41. The thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 24 to 38, wherein R^{4A} is substituted or unsubstituted phenyl, or substituted or unsubstituted thienyl.

42. The thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 24 to 38, wherein R^{4A} is phenyl.

43. A medicament comprising the thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 24 to 42 as an active ingredient.

44. A mitotic kinesin Eg5 inhibitor comprising the thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 24 to 42 as an active ingredient.

45. A therapeutic agent for a disease involving cell proliferation comprising the thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 24 to 42 as an active ingredient.

46. An antitumor agent comprising the thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 24 to 42 as an active ingredient.

47. A method for therapeutic and/or preventive treatment of a malignant tumor which comprises administering an effective amount of the thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 1 to 22.

48. A method for inhibiting a mitotic kinesin Eg5 which comprises administering an effective amount of the thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 1 to 22.

49. Use of the thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 1 to 22 for the manufacture of an

antitumor agent.

50. Use of the thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 1 to 22 for the manufacture of a mitotic kinesin Eg5 inhibitor.

51. A method for inhibiting a mitotic kinesin Eg5 which comprises administering an effective amount of the thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 24 to 42.

52. A method for therapeutic and/or preventive treatment of a disease involving cell proliferation which comprises administering an effective amount of the thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 24 to 42.

53. A method for therapeutic and/or preventive treatment of a malignant tumor which comprises administering an effective amount of the thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 24 to 42.

54. Use of the thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 24 to 42 for the manufacture of a mitotic kinesin Eg5 inhibitor.

55. Use of the thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 24 to 42 for the manufacture of a therapeutic agent for a disease involving cell proliferation.

56. Use of the thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 24 to 42 for the manufacture of an antitumor agent.